

## Clinical and polysomnographic features of patients with Restless Legs Syndrome

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### Abstract

**Objective:** To reveal clinical and polysomnographic features in patients treated for restless leg syndrome, and to examine the compatibility of sleep data and clinical features.

**Methods:** The study was conducted at the Department of Neurology, Ankara Numune Training and Education Hospital, Ankara, Turkey, and comprised patients who presented to the outpatient clinic between January and July 2014 who were diagnosed with restless leg syndrome based on the International Restless Leg Syndrome Study Group criteria. Patients underwent polysomnography test in spontaneous sleep in a single room. SPSS 18 was used for statistical analyses.

**Results:** Of the 18 patients, 13(72%)were females and 5(28%)were males. Overall mean age was 51.56±11.57years (range: 23-66 years). Fourteen (77.8%) patients reported insomnia; 10(55.5%) patients had excessive daytime sleepiness; 13(72.2%) reported snoring; and 3(17%) had apnoea. Mean International Restless Legs Syndrome Study Group Rating Scale score was 26.11±7.9 (range: 16-40).Mean Epworth Sleepiness Scale score was 9.17±5.1 (range: 0-20).

**Conclusion:** Restless leg syndrome was more common in women and the most common complaint was insomnia.

**Keywords:** Restless legs syndrome, Polysomnography, Sleep disorder. (JPMA 66: 568; 2016)

### Introduction

Restless legs syndrome (RLS) is a sensorimotor neurological disease which significantly affects the quality of life and manifests as a sensation of intolerable discomfort in the legs and paresthesia.<sup>1,2</sup> Its reported incidences range between 5% and 15%, even reaching up to 25% in general Western population. RLS is more common in women by two folds than in men. Its incidence has been found to be lower in Asian societies.<sup>1-4</sup> The disease is frequent and severe enough to require medical treatment in approximately 3% of the population.<sup>5</sup> According to the International Restless Leg Syndrome Study Group (IRLSSG), basic diagnostic criteria include: uncomfortable sensation in the legs, occurring or worsening of this sensation during sitting and rest, and resolution or alleviation of the symptoms with movement, further worsening of the symptoms in the evening and at night, and excluding the condition that may mimic RLS.<sup>2,6,7</sup> Treatment strategies differ according to severity of the disease. Different treatment options are offered for the patient group with paroxysmal and mild symptoms, while other options are used for the constant and resistant symptoms. Non-pharmacological treatment can be used in the mild-symptoms group. Patients are

advised to pay attention to sleep hygiene and avoid substances worsening the symptoms such as alcohol, nicotine and caffeine.<sup>8-10</sup> Regular daily exercise and activities have been reported to be helpful in the mild-symptoms group.<sup>11</sup> Non-pharmacological options are insufficient in the moderate and severe patient groups and these patients require pharmacological therapy. The first option in this group is dopa agonists.<sup>12</sup> In addition, levodopa-carbidopa, gabapentin, low-potency opioids or opioids receptor agonists can be administered.<sup>8,9,13</sup>

RLS is frequently associated with insomnia.<sup>14</sup> Polysomnography (PSG) is not recommended to be routinely used for the diagnosis of RLS. In the studies conducted with PSG, single-night tests in RLS patients yielded periodic limb movements of sleep (PLMS) by 70-80% and PLMS index by 5 or higher in adults. Using multiple PSGs, number of PLMSs per hour was found to be 5 or higher in 90% RLS patients. Some PLMSs cause arousals which may impair sleep hygiene.<sup>15</sup>

The current study was planned to reveal clinical and PSG features in RLS patients, and to examine the compatibility of sleep data and clinical features.

### Patients and Methods

The study was conducted at the Department of Neurology, Ankara Numune Training and Education Hospital, Ankara, Turkey, and comprised patients who presented to the outpatient clinic between January and July 2014, and were diagnosed with RLS based on the

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IRLSSG criteria. After approval was obtained from the institutional ethics committee And written informed consent was obtained from the subjects, patients were asked to fill a questionnaire which included the following questions: "How old were you when the disease began?", "How do you describe your complaints?", "Do your complaints alleviate with movement?", "What time of day the complaints begin?", "How many days a week do you have these complaints?", "What do you do to relieve your complaints?", "Do you have similar complaints in your arms?" and "How was the course of disease over time?". Patients filled the International Restless Legs Syndrome Study Group Rating Scale (IRLS) proforma which consists of 10 questions (Table-1). To assess the association between sleep disturbance and RLS, the Epworth Sleepiness Scale (ESS) was filled (Table-2). It was also questioned whether they had any comorbid disease. Detailed neurological and otorhinolaryngologic examinations were carried out. Detailed neurological examination and electromyography (EMG) were performed in order to rule out additional pathologies such as peripheral neuropathy and radiculopathy. Serum levels of iron, iron-binding capacity, ferritin, calcium, sodium, magnesium, vitamin B12, folic acid, haemogram and thyroid function were studied. Patient with iron deficiency, vitamin deficiency, thyroid dysfunction, renal failure and peripheral neuropathy were excluded.

Patients underwent PSG in spontaneous sleep in a single room in the hospital's Sleep Center under the supervision of technicians. Audio and video recordings were taken through the whole night (Alice 5 Model PSG device). Four-channel electroencephalogram (EEG), electromyogram (EMG-submental and right-left tibialis), two-channel electrooculogram (EOG - right-left), electrocardiogram (ECG), nasal airflow, thorax and abdominal respiratory movements, pulse oximetry, blood oxygen saturation and body position data were recorded throughout the night during PSG. Data of all the patients were manually scored by the same specialist who had been certificated for sleep disorders. Scoring of PSG data was carried out in line with the second version of scoring guideline published by American Academy of Sleep Medicine (AASM) in 2012.<sup>16</sup> Sleep efficiency, sleep latency, distribution of sleep stages, Apnoea Hypopnoea Index (AHI), AHI during the rapid eye movement (REM) stage, AHI during the non-REM stage, minimal oxygen saturation, duration of the oxygen saturation lower than 90%, number and index of the leg movement, number and index of the periodical leg movement and, number and index of the leg movement which led to arousal were recorded. Leg EMG activities observed during the respiratory events in obstructive sleep apnoea syndrome (OSAS) patients were not marked

as legs movement, as specified in the AASM guidelines. Only EMG activities which should be marked as leg movement based on the criteria included in the AASM guideline which are independent of the respiratory events were marked in OSAS patients.

In addition, the patients were also asked about the treatments they had received, the length and dosage of the treatment and whether they had benefited from treatment.

Data obtained through patient history and the questionnaires was compared with PSG results statistically.

Statistical analysis was done using SPSS 18. Compliance of the variables with normal distribution was studied using visual (histogram and probability plots) and analytical methods (Kolmogorov-Smirnov, Shapiro-Wilk tests). Correlation coefficients and statistical significance was calculated through Pearson correlation analysis in case of both variables showed normal distribution. Spearman test was used to estimate coefficients and statistical significance for the correlation between variables at least one of which showed non-normal distribution or was ordinal. Correlation between the nominal-nominal and nominal-continuous variables was interpreted using phi and eta correlation coefficients. Level of statistical significance was accepted as type-1 error level of 5%.

## Results

Of the 18 patients, 13(72%) were females and 5(28%) were males. Overall mean age was  $51.56 \pm 11.57$  years (range: 23-66 years). Ten (55.6%) patients had family history (55.6%), 6(33.3%) had hypertension (HT) and 2(11.1%) had arrhythmia. Complaints were localised only in the legs in 13(72.2%) patients, while 5(27.8%) had complaints in the arms also. Nine (50%) patients had complaints only at night. Complaints had begun in 10(55.6%) patients at age 45 years or less (mean:  $35.20 \pm 11.94$  years; range: 10-45 years) and at over 45 years in 8(44.4%) patients (mean:  $56.75 \pm 5.49$  years; range: 49-64 years).

Overall, 14(77.8%) patients reported insomnia; 10(55.6%) had excessive daytime sleepiness; 13(72.2%) had snoring; and 3(16.7%) had apnoea.

Mean IRLS score was  $26.11 \pm 7.9$  (range: 16-40). Mean ESS score was  $9.17 \pm 5.1$  (range: 0-20).

PSG data showed mean sleep efficiency to be  $85.31 \pm 9.9$  (range: 54-96), mean REM sleep latency  $124.5 \pm 66.3$  (range: 5.5-316), mean Stage N3 sleep latency  $17 \pm 11.7$  (range: 1.8-43.5), mean total sleep time  $357.4 \pm 53.7$  (range: 223-412.5), mean Stage N1 percentage  $5.8 \pm 4.6$

**Table-1:** International Restless Legs syndrome study group rating scale.

Have the patient rate his/her symptoms for the following ten questions. The patient and not the examiner should make the ratings, but the examiner should be available to clarify any misunderstandings the patient may have about the questions. Either the examiner or the patient may mark the answers on the form.

1. Overall, how would you rate the RLS discomfort in you legs or arms?  
(4) Very severe (3) Severe (2) Moderate (1) Mild (0) None
2. Overall, how would you rate the need to move around because of your RLS symptoms?  
(4) Very severe (3) Severe (2) Moderate (1) Mild (0) None
3. Overall, how much relief of your RLS arm or leg discomfort do you get from moving around?  
(4) No relief (3) Slight relief (2) Moderate relief (1) Either complete or almost complete relief  
(0) No RLS symptoms and therefore question does not apply
4. Overall, how severe is your sleep disturbance from your RLS symptoms?  
(4) Very severe (3) Severe (2) Moderate (1) Mild (0) None
5. How severe is your tiredness or sleepiness from your RLS symptoms?  
(4) Very severe (3) Severe (2) Moderate (1) Mild (0) None
6. Overall, how severe is your RLS as a whole?  
(4) Very severe (3) Severe (2) Moderate (1) Mild (0) None
7. How often do you get RLS symptoms?  
(4) Very severe (This means 6 to 7 days a week.)  
(3) Severe (This means 4 to 5 days a week.)  
(2) Moderate (This means 2 to 3 days a week.)  
(1) Mild (This means 1 day a week or less.)  
(0) None
8. When you have RLS symptoms, how severe are they on an average day?  
(4) Very severe (This means 8 hours per 24 hour day or more.)  
(3) Severe (This means 3 to 8 hours per 24 hour day.)  
(2) Moderate (This means 1 to 3 hours per 24 hour day.)  
(1) Mild (This means less than 1 hour per 24 hour day.)  
(0) None
9. , how severe is the impact of your RLS symptoms on your ability to carry out your , for example carrying out a satisfactory family, home, social, school, or work life? Overall daily affairs  
(4) Very severe (3) Severe (2) Moderate (1) Mild (0) None
10. How severe is the impact of your RLS symptoms — on your mood disturbance — for example angry, depressed, sad, anxious, or irritable?  
(4) Very severe (3) Severe (2) Moderate (1) Mild (0) None

(range: 1.8-20.9), mean Stage N2 percentage 48.4±16.6 (range: 17-77), mean Stage N3 percentage 25.02±14.06 (range: 1.8- 51.5), mean REM percentage 20.1±9.2 (8.5-41.3), mean AHI value 11.01±10.5 (range: 2-43), mean REM AHI 16.4±22.6 (range: 0-82.1), mean non-REM AHI 9.9±10.4 (range: 1.2-39.1); and mean oxygen saturation 85.1±7.6 (range: 64-94%).

Mean total number of leg movement was 108.2±150.6 (range: 3-593), mean leg movement index was 18.9±28.3 (range: 0.5-115.5), mean number of leg movement causing arousals was 32.3±57.6 (range: 0-214), and mean arousal-related legs movement index was 5.76±10.7

**Table-2:** The Epworth Sleepiness Scale (ESS).

How likely are you to doze off or fall asleep in the following situations, in contrast to feeling just tired? This refers to your usual way of life in recent times. Even if you have not done some of these things recently try to work out how they would have affected you. Use the following scale to choose the most appropriate number for each situation:

0 = would never doze

1 = slight chance of dozing

2 = moderate chance of dozing

3 = high chance of dozing

**Situation Chance of Dozing (0-3)**

Sitting and reading

Watching television

Sitting inactive in a public place (e.g. a theater or meeting)

As a passenger in a car for an hour without a break

Lying down to rest in the afternoon when circumstances permit

Sitting and talking to someone

Sitting quietly after a lunch without alcohol

In a car, while stopped for a few minutes in the traffic

(range: 0-41.7).

Accordingly, OSAS was identified in 9(50%) patients.

Mean periodical leg movement index was 15.7±28.9 (range: 0-114.9).

All the 18(100%) patients were receiving medical treatment. Among them, 17(94.4%) patients were using pramipexole and 1(5.6%) patient gabapentin. Dose of pramipexole was 2 mg/day in 1(5.6%) patient, 1mg/day in 2(11.3%), 0.5mg/day in 9(50%), 0.250mg/day in 4(45%), and 0.125mg/day in 1(5.6%) patient. Eleven (61%) patients stated that they had a lot of benefit from the treatment, while 3(16.7%) patients had not benefited.

On statistical comparison, a moderately significant negative correlation was found between sleep efficiency and IRLS scores. Sleep efficiency decreased as did IRLS scores, meaning that subjective complaints of patients increased ( $p=0.044$ ).

A perfect correlation between sleep efficiency and insomnia variables was identified. It was found that sleep efficiency was lower in patients who had complaints of insomnia ( $p=0.029$ ).

A perfect correlation between Stage N3 and REM percentage variables was identified. It was observed in objective PSG recordings that State N3 and REM sleep decreased in patients who had complaints of insomnia ( $p=0.021$ ,  $p=0.030$ ).

A moderately significant positive correlation was found between REM sleep latency and ESS variables REM sleep latency prolonged as ESS score increased ( $p=0.049$ ).

A perfect correlation between REM sleep latency and insomnia variables was identified at a significant level. REM sleep latency was longer in patients who had complaints of insomnia ( $p=0.032$ ).

Stage N3 percentage was moderately negatively correlated with total number of leg movements ( $p=0.044$ ), total leg movement index ( $p=0.035$ ), number of periodical leg movements ( $p=0.033$ ), periodical leg movements index ( $p=0.43$ ) and total time of periodical leg movement ( $p=0.032$ ). According to these parameters, deep sleep statistically decreased with worsening of all the leg movement parameters obtained on PSG.

A moderately significant positive correlation was found between IRLS and leg movements associated with arousal. Leg movements associated with arousal increased as IRLS scores worsened ( $p=0.042$ ).

A moderately significant negative correlation was found between IRLS scores and age variables. IRLS scores were better in advanced ages ( $p=0.019$ ).

A correlation between "age of the complaint onset" and "complaints in the arms?" variables was identified at a significant level. That is, presence of complaints elsewhere out of legs differed with aging with more common complaints in the patients in whom complaints had begun at a younger age ( $p=0.015$ ).

"Complaints in the arms?" variable was correlated with sleep efficiency, Stage N3 sleep latency, Stage N 1-2-3 percentages and total sleep time at significant levels. Presence of complaints in the arms were found to significantly affect almost all sleep data, while significant disturbances were observed in the sleep patterns of these patients ( $p=0.046$ ,  $p=0.007$ ,  $p=0.037$ ).

Drug benefits were found to be strongly negatively correlated with the number and total time of episodes of the periodical leg movements. In objective PSG data, number of leg movements was less in patients who specified that they had benefited from treatment ( $p=0.004$ ,  $p=0.035$ ).

## Discussion

Diagnosis of RLS can be established based on the IRLSSG diagnostic criteria. Basic criteria that should be found in RLS patients include uncomfortable sensation in the legs, occurring or worsening of this sensation during sitting and rest and resolution or alleviation of the symptoms with movement, further worsening of the symptoms in the evening and at night, and excluding the condition that may mimic RLS.<sup>2,6,7</sup> We also set the diagnosis of RLS based on these criteria.

RLS disease may begin in all age groups. Data in literature indicates that the disease may be seen between the age range of 6 and 80 years.<sup>15-19</sup> In our patients, onset of the complaints was between 10 and 64 years of age.

RLS is more commonly seen in women. It has been reported in literature that incidence of RLS is two times higher in women compared to men.<sup>1-3</sup> In our study, consistent with the literature incidence of RLS was higher in female patients by a F/M rate of 2.2/1.

Family history is accepted as a supportive criterion for RLS diagnosis. Family histories between 3.2% and 50% have been reported in literature.<sup>18,21</sup> Family history reaches 77% especially in RLS patients in whom onset of the complaints had begun in the childhood period.<sup>19</sup> In our study, family history was found by 44.4%.

Apart from the legs, complaints of RLS may also be seen in the arms. This condition has been reported between 42.8% and 48.7% in literature.<sup>21,22</sup> In this study, complaints in the arms were observed in 5(27.8%)patients.

Complaints of sleep disorders, failure to sleep enough and insomnia are among the most common complaints. Complaints of sleep problems have been reported in literature between 47.9% and 53%.<sup>23,24</sup> Of our patients, 77.8% had complaints of sleep disorders.

Although daytime sleepiness is among the most encountered complaints, ESS scores have been reported within the normal limits. In this study, we found ESS scores between 0 and 20 (mean  $9.17\pm 5.19$ ).<sup>25,26</sup>

Iron deficiency, pregnancy and renal failure are the most important conditions that may cause RLS. Patients having these conditions are considered as secondary RLS. We excluded the patients with additional pathologies that may lead to RLS.

IRLS scores are a gold standard scale with proven validation.<sup>27,28</sup> The scores between 31 and 40 are accepted as very severe, 21-30 as severe, 11-20 as moderate and 1-10 as mild. In this study, we found the IRLS scores between 16 and 40 with a mean value of  $26.11\pm 7.95$ .

PSG is not necessary to establish diagnosis of RLS. However, PSG provides valuable information for determination of additional sleep disturbances like OSAS, differential diagnosis of parasomnia or for assessment of the correlation of subjective findings. Some studies demonstrated impaired sleep patterns, decreased sleep efficiency, prolongation of the sleep latency and increase in the number of awakenings in RLS patients, while others



reported that no significant difference was found in terms of PSG measurements (total sleep time, sleep efficiency, sleep and wakefulness time). In this study, significant decreases were observed especially in N3 sleep. It was found that deepness in sleep statistically decreased with worsening of all leg movement parameters. We also observed that sleep efficiency was correlated with IRLS scores and sleep efficiency was lower in patients with subjectively poor questionnaire outcomes.<sup>29,30</sup>

Among the sleep data, IRLS was significantly correlated especially with sleep efficiency and the number of leg movements associated with arousal ( $p=0.044$  and  $p=0.042$ ; respectively).

Periodical leg movement are common in RLS. In the studies conducted with single-night PSG, periodical leg movements were reported in 70-90% of RLS patients.<sup>15</sup> In our study group, periodical leg movement index was found as minimal 0 and maximal 114.9 with a mean value of  $15.7\pm 28.9$  and all patients were under treatment.

It was found that patients who had complaints also in the arms were more affected and this condition caused significant decrease in many PSG parameters (sleep efficiency, N3 sleep latency, REM sleep latency, N1, N2, N3 percentages, REM percentage and total sleep time).

OSAS may be seen in association with RLS and the incidence of this association has been reported in literature as 55.4%.<sup>23</sup> In some studies, OSAS patients have been excluded, considering they have secondary RLS. However, in PSG scoring periodical leg movements which are independent of respiratory events during sleep must be used. If patients with periodical leg movements independent of respiratory events meet diagnostic criteria of RLS in addition to OSAS, they should be considered OSAS in addition to RLS. In our study, rate of patients with OSAS in addition to RLS was 50%, consistently with the literature.<sup>23</sup>

Dopamin agonists, levodopa-carbidopa, gabapentin, low-potency opioids or opioids receptor agonists are used in treatment of RLS.<sup>8,9,12,13</sup> In this study, dopamin agonist (pramipexole) was used in 17 patients and gabapentin in 01 patient. Subjective evaluation of drug efficacy was statistically compatible with the leg movements identified on PSG.

## Conclusion

Consistent with literature, it was found in our study that RLS was more common in women, family history was frequently observed, and the most common complaint was insomnia. Disturbances in sleep efficiency and sleep

patterns was found in PSG examination of RLS patients. Complaints of the patients and disturbances in the sleep patterns in PSG were correlated with the questionnaire outcomes. Further disturbance was found in the sleep data in patients who had additional complaints in the arms. Association of RLS and OSAS may be commonly encountered. If this association is found, then evaluation with PSG must be made.

## References

1. Nagandla K, De S. Restless legs syndrome: Pathophysiology and modern management. *Postgrad Med J* 2013; 89: 402-10.
2. Yang JS, Cho YJ, Kang SH, Choi HJ. Demographic and clinical characteristics of patients with restless legs syndrome in spine clinic. *J Korean Neurosurg Soc* 2014; 55: 83-8.
3. Allen RP, Earley CJ. Restless legs syndrome: a review of clinical and pathophysiologic features. *J Clin Neurophysiol* 2011; 18: 128-47.
4. Budhijara P, Budhijara R, Goodwin JL, Allen RP, Newman AB, Koo BB, et al. Incidence of restless legs syndrome and its correlates. *J Clin Sleep Med* 2012; 8: 119-24.
5. Bogan RK, Cheray JA. Restless legs syndrome: a review of diagnosis and management in primary care. *Postgrad Med* 2013; 125: 99-111.
6. Hirata K, Suzuki K. [Diagnosis and novel treatment approaches in restless legs syndrome: I. Pathophysiology and diagnosis]. *Brain Nerve* 2013; 65:1185-97.
7. Allen RP, Picchiatti DL, Garcia-Borreguero D, Ondo WG, Walters AS, Winkelman JW, et al. International Restless Legs Syndrome Study Group. Restless legs syndrome/Willis-Ekbom disease diagnostic criteria: updated International Restless Legs Syndrome Study Group (IRLSSG) consensus criteria—history, rationale, description, and significance. *Sleep Med* 2014; 15: 860-73.
8. Symvoulakis E, Anyfantakis D, Lionis C. Restless legs syndrome: literature review. *Sao Paulo Med J* 2010; 128: 167-70.
9. Silber MH, Ehrenberg BL, Allen RP, Buchfuhrer MJ, Earley CJ, Hening WA et al. An algorithm for the management of restless legs syndrome. *Mayo Clin Proc* 2004; 79: 916-22.
10. Hening WA. Current guidelines and standards of practice for restless legs syndrome. *Am J Med* 2007; 120: S22-7.
11. Aukerman MM, Aukerman D, Bayard M, Tudiver F, Thorp L, Bailey B. Exercise and restless legs syndrome: a randomized controlled trial. *J Am Board Fam Med* 2006; 19: 487-93.
12. Hening WA, Allen RP, Earley CJ, Picchiatti DL, Silber MH. Restless Legs Syndrome Task Force of the Standards of Practice Committee of the American Academy of Sleep Medicine. An update on the dopaminergic treatment of restless legs syndrome and periodic limb movement disorder. *Sleep* 2004; 27: 560-83.
13. Spolador T, Allis JC, Ponde MP. Treatment of restless legs syndrome. *Rev Bras Psiquiatr* 2006; 28: 308-15.
14. Babacan-Yildiz G, Gürsoy E, Kolukisa M, Karaköse F, Akkoyunlu EM, Celebi A, et al. Clinical and polysomnographic features of a large Turkish pedigree with restless leg syndrome and periodic limb movements. *Sleep Breath* 2013; 17: 741-6.
15. Saletu B, Anderer P, Saletu-Zyhlarz GM. Recent advances in sleep research. *Psychiatr Danub* 2013; 25: 426-34.
16. Berry RB, Brooks R, Gamaldo CE, Harding SM, Lloyd RM, Marcus CL, et al. American Academy of Sleep Medicine. The AASM Manual for the Scoring of Sleep and Associated Events: Rules, Terminology and Technical Specifications, Version 2.0.3. [online] [cited 2014 July 25]. Available from: URL: [www.aasmnet.org](http://www.aasmnet.org)
17. Silber MH, Becker PM, Earley C, Garcia-Borreguero D, Ondo WG; Medical Advisory Board of the Willis-Ekbom Disease Foundation. Willis-Ekbom Disease Foundation revised consensus statement on

- the management of restless legs syndrome. *Mayo Clin Proc* 2013; 88: 977-86.
18. Furudate N, Komada Y, Kobayashi M, Nakajima S, Inoue Y. Daytime dysfunction in children with restless legs syndrome. *J Neurol Sci* 2014; 15; 336: 232-6.
  19. Picchietti DL, Bruni O, de Weerd A, Durmer JS, Kotagal S, Owens JA, et al. International Restless Legs Syndrome Study Group (IRLSSG). Pediatric restless legs syndrome diagnostic criteria: an update by the International Restless Legs Syndrome Study Group. *Sleep Med* 2013; 14: 1253-9.
  20. Stefanidis I, Vainas A, Dardiotis E, Giannaki CD, Gourli P, Papadopoulou D, et al. Restless legs syndrome in hemodialysis patients: an epidemiologic survey in Greece. *Sleep Med* 2013; 14: 1381-6.
  21. Chabli A, Michaud M, Montplaisir J. Periodic arm movements in patients with the restless legs syndrome. *Eur Neurol* 2000; 44: 133-8.
  22. Michaud M, Chabli A, Lavigne G, Montplaisir J. Arm restlessness in patients with restless legs syndrome. *Mov Disord* 2000; 15: 289-93.
  23. PLin SW, Chen YL, Kao KC, Yang CT, Chuang LP, Chou YT, et al. Diseases in patients coming to a sleep center with symptoms related to restless legs syndrome. *PLoS One* 2013; 19: 8.
  24. Anand S, Johansen KL, Grimes B, Kaysen GA, Dalrymple LS, Kutner NG, et al. Physical activity and self-reported symptoms of insomnia, restless legs syndrome, and depression: the comprehensive dialysis study. *Hemodial Int* 2013; 17: 50-8.
  25. Civelek GM, Ciftkaya PO, Karatas M. Evaluation of restless legs syndrome in fibromyalgia syndrome: an analysis of quality of sleep and life. *J Back Musculoskelet Rehabil* 2014; 27: 537-44.
  26. Dikici S, Bahadir A, Baltaci D, Ankarali H, Eroglu M, Ercan N, et al. Association of anxiety, sleepiness, and sexual dysfunction with restless legs syndrome in hemodialysis patients. *Hemodial Int* 2014; 18: 809-18.
  27. Walters AS, LeBrocq C, Dhar A, Hening W, Rosen R, Allen RP, et al. Validation of the International Restless Legs Syndrome Study Group rating scale for restless legs syndrome. *Sleep Med* 2003; 4: 121-32.
  28. Allen R, Oertel W, Walters A, Benes H, Schollmayer E, Grieger F, et al. Relation of the International Restless Legs Syndrome Study Group rating scale with the Clinical Global Impression severity scale, the restless legs syndrome 6-item questionnaire, and the restless legs syndrome-quality of life questionnaire. *Sleep Med* 2013; 14: 1375-80.
  29. Montplaisir J, Boucher S, Poirier G, Lavigne G, Lapierre O, Lespérance P. Clinical, polysomnographic, and genetic characteristics of restless legs syndrome: a study of 133 patients diagnosed with new standard criteria. *Mov Disord* 1997; 12: 61-5.
  30. Wetter TC, Stiasny K, Kohnen R, Oertel WH, Trenkwalder C. Polysomnographic sleep measures in patients with uremic and idiopathic restless legs syndrome. *Movement Disorders* 1998; 13: 820-4.
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